REMARKS

Upon entry of the foregoing amendments, the specification has been amended to remove URLs from the specification. No new matter has been added by the amendments to the specification.

The claims have been amended as set forth above. Claims 22-35 and 38-41 are pending. Claims 36-37 have been cancelled. Claims 22-30, 32-33 and 35 have been amended to remove reference to the Figures. Claims 22-27, 30 and 35 have been further amended to specify the particular amino acid sequence of the "extracellular domain." Support for this amendment is found, for example, in Figure 20. Also, Claims 22-26 and 35 have been amended to add the limitation that the claimed nucleic acids encode polypeptides that have the ability to induce chondrocyte redifferentiation. Support for this amendment is found in Example 36 on page 166, describing a chondrocyte redifferentiation assay (Assay #110). Also, Claim 35 has been amended to recite the specific hybridization conditions. The amendment to Claim 35 is supported by the specification at page 80, lines 10-14. Thus, no new matter is added by the amendments and the claims are fully supported by the specification as originally filed.

Applicants respond below to the specific rejections raised by the PTO in the Office Action mailed September 9, 2004. For the reasons set forth below, Applicants respectfully traverse.

Information Disclosure Statement

The Examiner asserts that the previously-filed information disclosure statement fails to comply with 37 C.F.R. § 1.98(a)(2). The Examiner notes that the Blast results are not true publications with a publication date, and therefore, are not fully in compliance with 37 C.F.R. § 1.97.

Respectfully, Applicants disagree. The Blast results are true publications with a publication date or other information consistent with the duty of disclosure and § 1.98(a)(2). The contents of the previously filed IDS, which has been objected to, satisfied the requirements of § 1.98(a)(2) because the IDS included a legible copy of each publication or that portion which caused it to be listed and all other information or that portion which caused it to be listed. In particular, the previously filed Blast results were legible, provided a comparison of a claimed sequence to another sequence, and showed the relevant information for the other sequence.

Nonetheless, for the convenience of the Examiner, more detailed information is submitted as Exhibit 1. The resubmitted results include more detailed information regarding the cited sequences. These Blast results are resubmitted before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application. Applicants believe that no fee is due because of compliance with §§ 1.97-1.98. However, if a fee is due to ensure consideration of the submitted Blast results, for example, the fee under § 1.17(p), the Patent Office is authorized to charge the fee to Deposit Account No. 11-1410.

Specification

The Examiner states that the specification should be reviewed for the recitation of improper hyperlinks, and that all such recitations should be deleted or amended. Applicants have amended the specification to address the Examiner's concern. In particular, Applicants have replaced the hyperlinks with text that describes the location of the websites. The amended text no longer constitutes browser executable code.

Rejection under 35 U.S.C. §101 - Utility

The Examiner rejects Claims 22-41 as allegedly not being supported by a specific and substantial asserted utility, or a well established utility. The Examiner notes that the "claims are directed to isolated polynucleotides encoding polypeptides corresponding to SEQ ID NO:45, and referred to in the specification as PRO4405." The Examiner argues that "one cannot extrapolate what constitutes a specific utility for the polynucleotides that encode polypeptides related to SEQ ID NO:45, because the specific 'qualitative biological activity' for even the encoded polypeptide depicted as SEQ ID NO:45 is not known, nor specifically described within the specification." According to the Examiner, the specification generally does assert various utilities for all of the disclosed encoded polypeptides, and general utilities for any polynucleotide, however, the Examiner argues that such utilities are generically possessed by any polypeptide or any polynucleotide. Therefore, the Examiner argues that none of the asserted utilities are specific for the claimed PRO4405 polynucleotides or encoded polypeptides. Furthermore, the Examiner argues that the asserted utilities are not "substantial," stating that the specification has assigned no specific activity to PRO4405.

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." A utility is "specific" when it is particular to the subject matter claimed. With regard to substantial utility, "[a]ny reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility." (M.P.E.P. 2107.01). "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record ... that is probative of the Applicant's assertions." (M.P.E.P. 2107 II(B)(1)(ii)). Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Respectfully, the claimed polynucleotides and the encoded polypeptides have a specific, substantial and credible utility as set forth in Example 36 of the specification on page 166. Example 36 describes a chondrocyte redifferentiation assay (Assay 110). This assay shows that certain polypeptides act to induce redifferentiation of chondrocytes, and therefore, are useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. As mentioned in Example 36, PRO4405 is one of the polypeptides that tested positive in the chondrocyte redifferentiation assay. Thus, contrary to the Examiner's statement, Applicants have provided a specific "qualitative biological activity" for the polypeptide depicted as SEQ ID NO:45.

The ability to induce chondrocyte redifferentiation is specific or particular to the PRO4405 polypeptides, and is not an ability common to all peptides generally. Also, the utility is substantial because treatment of bone and/or cartilage disorders provides a public benefit, and is a "real world" utility for the claimed polynucleotides. Finally, one of ordinary skill in the art would recognize that the scientific assay results of Example 36 support the credibility of the asserted utility. Therefore, the claimed polynucleotides have a specific, substantial and credible utility.

For the reasons discussed above, Applicants respectfully request reconsideration and withdrawal of the instant rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. §112, first paragraph – Enablement

The Examiner rejected Claims 22-41 under 35 U.S.C. § 112, first paragraph. According to the Examiner, because the claimed invention is not supported by either a substantial asserted utility or a well established utility, one of skill in the art would not know how to use the invention.

Applicants submit that in the above discussion of the rejection under 35 U.S.C. § 101, Applicants have established a substantial, specific, and credible utility for the claimed polynucleotides. Specifically, the PRO4405 polypeptides encoded by the claimed polynucleotides have utility in inducing chondrocyte redifferentiation.

Also, as set forth above, Claims 22-26 and 35 have been amended to recite the functional limitation "wherein said isolated nucleic acid encodes a polypeptide that has the ability to induce chondrocyte redifferentiation." In view of this, the specification teaches how to make and use the claimed subject matter. In particular, the specification describes how to make the claimed polynucleotides and how to assay for the function in the encoded polypeptides. Based upon that teaching and the above-established utility for the claimed subject matter, one skilled in the art would know how to make and use the claimed subject matter.

Therefore, Applicants therefore request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph, based on a lack of utility.

Rejections under 35 U.S.C. §112, first paragraph – Written Description

The Examiner asserts that Claims 22-27, 30-31 and 35-41 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner argues that "[n]o written description is provided in the specification for any other species of PRO4405 molecules, nor for any allelic and/or splice variants thereof (i.e., including molecules encoding polypeptides "having at least 80%, 85%, 90%, 95% or 99% amino acid sequence identity to SEQ ID NO:45), nor for any encoded polypeptides merely 'compris[ing]' 'extracellular domains of the polypeptide,' nor any encoded chimeric polypeptides thereof, nor for any random or generic polynucleotide that merely hybridize[s] to such)." Furthermore, the Examiner argues that such claims are not described

because the claims do not require that the polynucleotides possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature.

Applicants have amended Claims 22-26 and 35 to recite that the claimed nucleic acids encode polypeptides that have "the ability to induce chondrocyte redifferentiation." Accordingly, Applicants maintain that the claims recite sufficient distinguishing characteristics for the claimed genus of polynucleotides. Based on the detailed description in the specification of the cloning and expression of variant nucleic acids encoding PRO4405 polypeptides, the description of the assay in Example 36, the actual reduction to practice of sequences SEQ ID NOs: 44 and 45, and the functional recitation in the instant claims, Applicants submit that one of skill in the art would know that Applicants possessed the claimed polynucleotides. Hence, Applicants respectfully request that the PTO reconsider and withdraw the written description rejection under 35 U.S.C. §112.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected Claims 22-27, 30-31 and 35-41 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner states that "what encoded amino acid residues constitute 'the extracellular domain' is unclear, because 'glycosylation sites' are indicated to exist on both sides of the transmembrane domain." Further according to the Examiner, if the encoded polypeptide possesses an extracellular domain, the recitation of "the extracellular domain ... lacking its associated signal sequence" is indefinite because a signal sequence is general not considered to be part of an extracellular domain.

Figure 20 discloses that the encoded polypeptide includes transmembrane domains at amino acids 58-76. In view of this, Claims 22-27, 30 and 35 have been amended to recite the specific region comprising the extracellular domains, namely, amino acids 77-310. Furthermore, Claims 22-27 and 35 have been amended and Claim 31 cancelled in order to delete reference to the "signal peptide" in connection with the "extracellular domain."

The Examiner also rejected Claims 35-37 under 35 U.S.C. § 112, second paragraph, as being indefinite because "it is unknown what metes and bounds 'stringent hybridization conditions' entail, in that it is unknown whether low, moderate or high stringent conditions are envisioned; nor what exactly defines these conditions."

As set forth above, Claim 35 has been amended to recite the particular stringent conditions.

In view of the above discussion, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. §102

The Examiner has rejected Claims 22-25, 31, 35-37 and 38-41 under 35 U.S.C. § 102(b) as being anticipated by Adams et al. (clone EST70856; Accession no. AA361388; April 21, 1997). According to the Examiner, Adams et al. teach an isolated human 5' cDNA clone which comprises a nucleic acid that is at least 80/85/90/95% identical to "a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in ... SEQ ID NO:45 ... lacking its associated signal sequence." Also, the Examiner argues that Adams et al. was cloned into a vector, and transfected into an *E. coli* host cell. Furthermore, the Examiner argues that Claims 35-37 are anticipated because the sequences of Adams et al. being 98% identical to nucleotide residues 144-397 of SEQ ID NO:44, would clearly hybridize to SEQ ID NO:44 under stringent conditions; and also comprises at least 10 nucleotides in length.

Respectfully, Adams et al. fails to anticipate any of the pending claims. As mentioned above, rejected Claims 31 and 36-37 have been cancelled without prejudice toward future prosecution. Therefore, the rejection of those claims is not further addressed herein.

Claims 22-27 also are not anticipated because the sequence of Adams et al. has far less than 80% sequence identity to the claimed sequences. For example, the sequence of Adams et al. has less than 11% sequence identity to the nucleic acid sequence of SEQ ID NO:44; less than 13% sequence identity to the sequence encoding the extracellular domain of SEQ ID NO:45; and less than 27% sequence identity to the sequence encoding the polypeptide of SEQ ID NO:45, both with and without its signal sequence.

Claim 35 is not anticipated because the sequence of Adams et al., having such low sequence identity as noted above, would not hybridize to the claimed sequence under the specified hybridization conditions. Furthermore, the sequence of Adams et al. does not encode a polypeptide having the ability to induce chondrocyte redifferentiation.

Respectfully, Applicants request reconsideration and withdrawal of the instant § 102 rejection in view of the above discussion.

Conclusion

The present application is believed to be in condition for allowance, and an early action to that effect is respectfully solicited. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 12/8/04

By: 

Marc T. Morley
Registration No. 52,051
Attorney of Record
Customer No. 30,313
(619) 235-8550

S:\DOCS\MTM\MTM-7305.DOC
111904

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Mon Jan 7 16:13:00 2002 [BLASTP 2.2.1 [Jul-12-2001], NCBI]
/home/ruby/va/Molbio/carpenda/tempids/p1.DNA84920 (310 aa)
/home/ruby/va/Molbio/carpenda/tempids/p1.DNA84920
Database: day (1,637,781 seqs, 402,203,456 aa) Jan 6, 2002 5:13 PM
Locus list: hum (349,801 seqs, 66,964,548 aa)
Matrix: BLOSUM62, T: 11, A: 40, X1: 16, X2: 38, X3: 64, S1: 41, S2: 71, eval: 10.
Gap Penalties: Existence: 11, Extension: 1

Sequences producing High-scoring Segment Pairs:		Score	Match	Pct	E-val
1 P_AAB87595	Human PRO4405 - Homo sapiens.	1617	310	100	e-179
2 P_AAY72877	Human PRO4405 protein encoded by DNA84920	1617	310	100	e-179
3 P_AAM93346	Human polypeptide, SEQ ID NO: 2891 - Homo	1617	310	100	e-179
4 P_AAB18918	novel polypeptide designated PRO4405 - Ho	1617	310	100	e-179

Dayhoff Protein Database (Rel 78, Mar 2004)
P_AAB87595 Human PRO4405 - Homo sapiens.
Length: 310 aa
Accession: P_AAB87595;
Species: Homo sapiens.
Keywords: Human; PRO protein; mapping; patent; GENESEQ patentdb.
Patent number: WO200116318-A2.
Publication date: 08-MAR-2001.
Filing date: 24-AUG-2000; 2000WO-US023328.
Priority: 01-SEP-1999; 99WO-US020111. 15-SEP-1999; 99WO-US021090.
07-DEC-1999; 99US-0169495P. 09-DEC-1999; 99US-0170262P.
11-JAN-2000; 2000US-0175481P. 18-FEB-2000; 2000WO-US004341.
18-FEB-2000; 2000WO-US004342. 22-FEB-2000; 2000WO-US004414.
01-MAR-2000; 2000WO-US005601. 03-MAR-2000; 2000US-0187202P.
21-MAR-2000; 2000US-0191007P. 30-MAR-2000; 2000WO-US008439.
25-APR-2000; 2000US-0199397P. 22-MAY-2000; 2000WO-US014042.
05-JUN-2000; 2000US-0209832P.
Assignee: (GETH) GENENTECH INC.
Inventors: Eaton DL, Filvaroff E, Gerritsen ME, Goddard A, Godowski PJ;
Grimaldi CJ, Gurney AL, Watanabe CK, Wood WI;
Cross reference: WPI; 2001-183260/18. N-PSDB; AAF92127.
Title: Eighty four nucleic acids encoding PRO polypeptides, useful in
molecular biology, including use as hybridization probes, and in
chromosome and gene mapping.
Patent format: Claim 12; Fig 140; 278pp; English.
Comment: The present sequence is a human PRO polypeptide (secreted and
transmembrane). The PRO protein, and PRO agonists, PRO antagonists
or anti-PRO antibodies are useful for preparation of a medicament
useful in the treatment of a condition which is responsive to the
PRO protein, agonists, antagonists or anti-PRO antibodies. The PRO
protein may also be employed as molecular weight markers for
protein electrophoresis. The PRO coding sequence has applications
in molecular biology, including use as hybridisation probes, and in
chromosome and gene mapping
Database: GENESEQ patent database (v200423, 04-NOV-2004).

P_AAY72877 Human PRO4405 protein encoded by DNA84920-2614 cDNA clone -
Homo sapiens.
Length: 310 aa
Accession: P_AAY72877;
Species: Homo sapiens.
Keywords: Human; PRO4405; antiinflammatory; dermatological;
immunosuppressive; antirheumatic; antiarthritic; osteopathic;

antianaemic; haemostatic; antithyroid; antidiabetic; antiviral; antipsoriatic; antiallergic; antiasthmatic; inhibitor; therapy; systemic lupus erythematosis; spondyloarthropathy; systemic sclerosis; systemic vasculitis; sarcoidosis; idiopathic inflammatory myopathy; Sjogren's syndrome; autoimmune thrombocytopenia; immune-mediated renal disease; hepatitis; demyelinating polyneuropathy; Guillian-Barre syndrome; Whipple's disease; hepatobiliary disease; primary biliary cirrhosis; sclerosing cholangitis; inflammatory bowel disease; gluten-sensitive enteropathy; skin disease; allergic rhinitis; atopic dermatitis; food hypersensitivity; urticaria; eosinophilic pneumonia; hypersensitivity pneumonitis; graft rejection; idiopathic pulmonary fibrosis; graft-versus-host-disease; patent; GENESEQ patentdb.

Patent number: WO200116319-A2.

Publication date: 08-MAR-2001.

Filing date: 23-AUG-2000; 2000WO-US023522.

Priority: 31-AUG-1999; 99US-0151733P. 01-SEP-1999; 99WO-US020111. 16-DEC-1999; 99WO-US030095. 18-FEB-2000; 2000WO-US004342. 01-MAR-2000; 2000WO-US005601. 30-MAR-2000; 2000WO-US008439. 17-MAY-2000; 2000WO-US013705. 22-MAY-2000; 2000WO-US014042. 30-MAY-2000; 2000WO-US014941. 05-JUN-2000; 2000US-0209832P.

Assignee: (GETH) GENENTECH INC.

Inventors: Goddard A, Godowski PJ, Gurney AL, Hillan KJ, Tumas D; Watanabe CK, Wood WI;

Cross reference: WPI; 2001-226690/23. N-PSDB; AAD02923.

Title: New PRO polypeptides for treating immune related and inflammatory diseases such as rheumatoid arthritis, systemic vasculitis, asthma, autoimmune hemolytic anemia, and diabetes mellitus.

Patent format: Claim 10; Fig 8; 118pp; English.

Comment: The present sequence is PRO4405 protein encoded by DNA84920-2614 cDNA clone. PRO protein, its agonist or antagonist or its antibody which are capable of enhancing or inhibiting the proliferation of T-lymphocytes or of increasing the infiltration of inflammatory cells into a tissue are useful in the diagnosis and treatment of immune-related diseases in mammals. The PRO protein is useful for treating systemic lupus erythematosis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathy, systemic sclerosis, idiopathic inflammatory myopathy, Sjogren's syndrome, systemic vasculitis, sarcoidosis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, demyelinating disease of the central or peripheral nervous system, idiopathic demyelinating polyneuropathy, Guillian-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, hepatobiliary disease, infectious or autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, Whipple's disease, autoimmune or immune-mediated skin diseases such as bullous skin disease, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis, hyper- sensitivity pneumonitis, transplantation associated diseases such as graft rejection or graft-versus-host-disease

1-34/Peptide

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6-12/Modified-site
/note= N-myristoylation site/
35-310/Protein
/label= Mature_human_PRO4405_protein/
52-58/Modified-site
/note= N-myristoylation site/
56-60/Modified-site
/note= Asn is N-glycosylated/
58-76/Domain
/label= Transmembrane_domain/
100-106/Modified-site
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125-131/Modified-site
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154-158/Modified-site
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194-198/Modified-site
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205-208/Binding-site
/note= Cell attachment sequence/
233-239/Modified-site
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270-276/Modified-site
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275-281/Modified-site
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278-284/Modified-site
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Database: GENESEQ patent database (v200423, 04-NOV-2004).

P_AAM93346 Human polypeptide, SEQ ID NO: 2891 - Homo sapiens.
Length: 975 aa
Accession: P_AAM93346;
Species: Homo sapiens.
Keywords: Human; full length cDNA; cDNA synthesis; oligo-capping; patent;
GENESEQ patentdb.
Patent number: EP1130094-A2.
Publication date: 05-SEP-2001.
Filing date: 07-JUL-2000; 2000EP-00114089.
Priority: 08-JUL-1999; 99JP-00194486. 11-JAN-2000; 2000JP-00118774.
02-MAY-2000; 2000JP-00183765.
Assignee: (HELI-) HELIX RES INST.
Inventors: Ota T, Nishikawa T, Isogai T, Hayashi K, Ishii S, Kawai Y;
Wakamatsu A, Sugiyama T, Nagai K, Kojima S, Otsuki T, Koga H;
Cross reference: WPI; 2001-524255/58. N-PSDB; AAK94266.
Title: 830 Primers useful for synthesizing full length cDNA clones and
their use in genetic manipulation.
Patent format: Claim 8; SEQ ID NO 2891; 1380pp + Sequence Listing; English.
Comment: The invention relates to primers for synthesising full length cDNA
clones. 830 cDNA molecules encoding a human protein have been
isolated and nucleotide sequences of 5'- and 3'-ends of the cDNA
molecules have been determined. Primers for synthesising the full
length cDNA are useful for clarifying the function of the protein
encoded by the cDNA. The full length clones were obtained by
construction of full length enriched cDNA libraries that were
synthesised by the oligo-capping method. The primers enable the

production of the full length cDNA easily without any special methods. The present sequence is a polypeptide encoded by a full length human cDNA of the invention. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in CD-ROM format directly from EPO

Database: GENESEQ patent database (v200423, 04-NOV-2004).

P_AAB18918 A novel polypeptide designated PRO4405 - Homo sapiens.
Length: 310 aa
Accession: P_AAB18918;
Species: Homo sapiens.
Keywords: Secreted protein; transmembrane protein; PRO1484; PRO4334; PRO1122; PRO1889; PRO1890; PRO1887; PRO1785; PRO4353; PRO4357; PRO4405; PRO4356; PRO4352; PRO4380; PRO4354; PRO4408; PRO5737; PRO4425; PRO5990; PRO6030; PRO4424; PRO4422; PRO4430; PRO4499; tumour; obesity; diabetes; insulinemia; kidney disorder; Bergers disease; nephropathy; Schonlein-Henoch purpura; celiac disease; dermatitis herpetiformis; Crohns disease; patent; GENESEQ patentdb.
Patent number: WO200056889-A2.
Publication date: 28-SEP-2000.
Filing date: 01-MAR-2000; 2000WO-US005601.
Priority: 23-MAR-1999; 99US-0125774P. 23-MAR-1999; 99US-0125778P. 24-MAR-1999; 99US-0125826P. 31-MAR-1999; 99US-0127035P. 05-APR-1999; 99US-0127706P. 21-APR-1999; 99US-0130359P. 27-APR-1999; 99US-0131270P. 27-APR-1999; 99US-0131272P. 27-APR-1999; 99US-0131291P. 04-MAY-1999; 99US-0132371P. 04-MAY-1999; 99US-0132379P. 04-MAY-1999; 99US-0132383P. 25-MAY-1999; 99US-0135750P. 08-JUN-1999; 99US-0138166P. 20-JUL-1999; 99US-0144791P. 03-AUG-1999; 99US-0146970P. 09-DEC-1999; 99US-0170262P.
Assignee: (GETH) GENENTECH INC.
Inventors: Desnoyers L, Eaton DL, Goddard A, Godowski PJ, Gurney AL, Pan J; Stewart TA, Watanabe CK, Wood WI, Zhang Z;
Cross reference: WPI; 2000-628263/60. N-PSDB; AAA96345.
Title: Novel secreted and transmembrane polypeptides useful for diagnosing tumor in a mammal, for identifying agonists and antagonists of the polypeptide and for therapeutic use.
Patent format: Claim 12; Fig 20; 222pp; English.
Comment: The present sequence represents a secreted or transmembrane polypeptide. The specification describes polypeptides designated PRO1484, PRO4334, PRO1122, PRO1889, PRO1890, PRO1887, PRO1785, PRO4353, PRO4357, PRO4405, PRO4356, PRO4352, PRO4380, PRO4354, PRO4408, PRO5737, PRO4425, PRO5990, PRO6030, PRO4424, PRO4422, PRO4430 and PRO4499. PRO1889 polypeptide is useful for diagnosing tumour in a mammal. The polypeptides, their agonists and antagonists are useful treating a condition associated with expression or activity of the polypeptide. Conditions treated include obesity, diabetes or hyper-or hypo-insulinemia. The polypeptides are capable of inducing proliferation of mammalian kidney mesangial cells and are therefore useful for treating kidney disorders associated with decreased mesangial cell function such as Bergers disease or other nephropathies associated with Schonlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohns disease. The nucleic acids may be used to generate transgenic animals for use in development and screening of therapeutically useful reagents and also for chromosome identification and tissue typing

1-34/Peptide
/note= signal peptide/
6-12/Modified-site
/note= N-myristoylation site/
52-58/Modified-site
/note= N-myristoylation site/
56-60/Modified-site
/note= N-glycosylation site/
58-76/Domain
/note= transmembrane domain/
100-106/Modified-site
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125-131/Modified-site
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154-158/Modified-site
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194-198/Modified-site
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233-239/Modified-site
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278-284/Modified-site
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Database: GENESEQ patent database (v200423, 04-NOV-2004).

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Repeats masked (summary below)
/home/ruby/va/Molbio/carpenda/tempids/ss.DNA84920 (2395 bp)
       /home/ruby/va/Molbio/carpenda/tempids/ss.DNA84920
Database: gen (16,229,280 seqs, 16,995,651,507 bp)  Jan 1, 2002  2:50 AM
   Locus list: hum -est (1,803,435 seqs, 6,559,376,613 bp)
Matrix: blastn matrix:1 -3, T: 0, A: 40, X1: 6, X2: 15, S1: 12, S2: 20, eval: 10.
Gap Penalties: Existence: 5, Extension: 2

Sequences producing High-scoring Segment Pairs:      Frame Score Match Pct E-val
  1 P_AAA96345 cDNA encoding a novel polypeptide design  +  2395  2395 100   0.0
  2 P_AAD02923 Human PRO4405 cDNA (DNA84920-2614). cDN  +  2395  2395 100   0.0
  3 P_AAF92127 Human PRO4405 cDNA.                      +  2395  2395 100   0.0
  4 P_AAC91490 Human PRO4405 cDNA.                      +  2395  2395 100   0.0
  5 AX089946   Sequence 7 from Patent WO0116319.  DNA,  +  2395  2395 100   0.0
  6 AX092408   Sequence 139 from Patent WO0116318.  DNA  +  2395  2395 100   0.0
  7 AX055478   Sequence 108 from Patent WO0073452.  DNA  +  2395  2395 100   0.0

GenBank (Release 143, aug 2004)

2395 100   0.0
P_AAA96345  cDNA encoding a novel polypeptide designated PRO4405. 395 bp,
          cDNA, PAT 08-FEB-2001
ACCESSION   P_AAA96345
KEYWORDS    GENESEQ; Secreted protein; transmembrane protein; PRO1484; PRO4334;
          PRO1122; PRO1889; PRO1890; PRO1887; PRO1785; PRO4353; PRO4357;
          PRO4405; PRO4356; PRO4352; PRO4380; PRO4354; PRO4408; PRO5737;
          PRO4425; PRO5990; PRO6030; PRO4424; PRO4422; PRO4430; PRO4499;
          tumour; obesity; diabetes; insulinemia; kidney disorder; Bergers
          disease; nephropathy; Schonlein-Henoch purpura; celiac disease;
          dermatitis herpetiformis; Crohns disease;  patent; patentdb
          (v200423, 04-NOV-2004).
SOURCE      Homo sapiens.
  ORGANISM  Homo sapiens.
REFERENCE   1  (bases 1 to 2395)
  AUTHORS   Desnoyers,L.,  Eaton,D.L.,  Goddard,A.,  Godowski,P.J.,
          Gurney,A.L.,  Pan,J. Stewart,T.A.,  Watanabe,C.K.,  Wood,W.I.,
          Zhang,Z.
  TITLE     Novel secreted and transmembrane polypeptides useful for diagnosing
          tumor in a mammal, for identifying agonists and antagonists of the
          polypeptide  and for therapeutic use.
  JOURNAL   Patent: WO200056889-A2; Filing Date: 01-MAR-2000; 2000WO-US005601;
          Publication Date: 28-SEP-2000; Priority: 23-MAR-1999;
          99US-0125774P. 23-MAR-1999;   99US-0125778P. 24-MAR-1999;
          99US-0125826P. 31-MAR-1999;   99US-0127035P. 05-APR-1999;
          99US-0127706P. 21-APR-1999;   99US-0130359P. 27-APR-1999;
          99US-0131270P. 27-APR-1999;   99US-0131272P. 27-APR-1999;
          99US-0131291P. 04-MAY-1999;   99US-0132371P. 04-MAY-1999;
          99US-0132379P. 04-MAY-1999;   99US-0132383P. 25-MAY-1999;
          99US-0135750P. 08-JUN-1999;   99US-0138166P. 20-JUL-1999;
          99US-0144791P. 03-AUG-1999;   99US-0146970P. 09-DEC-1999;
          99US-0170262P; Assignee: (GETH ) GENENTECH INC; Cross Reference:
          WPI; 2000-628263/60. P-PSDB; AAB18918; Patent Format: Claim 2; Fig
          19; 222pp; English.
COMMENT     The present sequence encodes a secreted or transmembrane
          polypeptide. The specification describes polypeptides designated
          PRO1484, PRO4334,  PRO1122, PRO1889, PRO1890, PRO1887, PRO1785,
          PRO4353, PRO4357, PRO4405,  PRO4356, PRO4352, PRO4380, PRO4354,
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PRO4408, PRO5737, PRO4425, PRO5990, PRO6030, PRO4424, PRO4422, PRO4430 and PRO4499. PRO1889 polypeptide is useful for diagnosing tumour in a mammal. The polypeptides, their agonists and antagonists are useful treating a condition associated with expression or activity of the polypeptide. Conditions treated include obesity, diabetes or hyper-or hypo-insulinemia. The polypeptides are capable of inducing proliferation of mammalian kidney mesangial cells and are therefore useful for treating kidney disorders associated with decreased mesangial cell function such as Bergers disease or other nephropathies associated with Schonlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohns disease. The nucleic acids may be used to generate transgenic animals for use in development and screening of therapeutically useful reagents and also for chromosome identification and tissue typing

FEATURES Location/Qualifiers
CDS 79..1011
/*tag= a
sig_peptide 79..180
/*tag= b
BASE COUNT 566 a 605 c 656 g 568 t
ORIGIN

2395 100 0.0
P_AAD02923 Human PRO4405 cDNA (DNA84920-2614). 395 bp, cDNA, PAT 31-MAY-2001
ACCESSION P_AAD02923
KEYWORDS GENESEQ; Human; PRO4405; antiinflammatory; dermatological; immunosuppressive; antirheumatic; antiarthritic; osteopathic; antianaemic; haemostatic; antithyroid; antidiabetic; antiviral; antipsoriatic; antiallergic; antiasthmatic; inhibitor; therapy; systemic lupus erythematosis; spondyloarthropathy; systemic sclerosis; systemic vasculitis; sarcoidosis; idiopathic inflammatory myopathy; Sjogren's syndrome; autoimmune thrombocytopenia; immune-mediated renal disease; hepatitis; demyelinating polyneuropathy; Guillian-Barre syndrome; Whipple's disease; hepatobiliary disease; primary biliary cirrhosis; sclerosing cholangitis; inflammatory bowel disease; gluten-sensitive enteropathy; skin disease; allergic rhinitis; atopic dermatitis; food hypersensitivity; urticaria; eosinophilic pneumonia; hypersensitivity pneumonitis; graft rejection; idiopathic pulmonary fibrosis; graft-versus-host-disease; patent; patentdb (v200423, 04-NOV-2004).
SOURCE Homo sapiens.
ORGANISM Homo sapiens.
REFERENCE 1 (bases 1 to 2395)
AUTHORS Goddard,A., Godowski,P.J., Gurney,A.L., Hillan,K.J., Tumas,D. Watanabe,C.K., Wood,W.I.
TITLE New PRO polypeptides for treating immune related and inflammatory diseases such as rheumatoid arthritis, systemic vasculitis, asthma, autoimmune hemolytic anemia, and diabetes mellitus.
JOURNAL Patent: WO200116319-A2; Filing Date: 23-AUG-2000; 2000WO-US023522; Publication Date: 08-MAR-2001; Priority: 31-AUG-1999; 99US-0151733P. 01-SEP-1999; 99WO-US020111. 16-DEC-1999; 99WO-US030095. 18-FEB-2000; 2000WO-US004342. 01-MAR-2000; 2000WO-US005601. 30-MAR-2000; 2000WO-US008439. 17-MAY-2000; 2000WO-US013705. 22-MAY-2000; 2000WO-US014042. 30-MAY-2000; 2000WO-US014941. 05-JUN-2000; 2000US-0209832P; Assignee: (GETH)

GENENTECH INC; Cross Reference: WPI; 2001-226690/23. P-PSDB; AAY72877; Patent Format: Claim 2; Fig 7; 118pp; English.

COMMENT The present sequence is a cDNA (DNA84920-2614 clone) encoding PRO4405 protein. PRO protein, its agonist or antagonist or its antibody which are capable of enhancing or inhibiting the proliferation of T-lymphocytes or of increasing the infiltration of inflammatory cells into a tissue are useful in the diagnosis and treatment of immune-related diseases in mammals. The PRO protein is useful for treating systemic lupus erythematosis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathy, systemic sclerosis, idiopathic inflammatory myopathy, Sjogren's syndrome, systemic vasculitis, sarcoidosis, autoimmune haemolytic anaemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, demyelinating disease of the central or peripheral nervous system, idiopathic demyelinating polyneuropathy, Guillian-Barre syndrome, chronic inflammatory demyelinating polyneuropathy, hepatobiliary disease, infectious or autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, Whipple's disease, autoimmune or immune-mediated skin diseases such as bullous skin disease, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis, hyper- sensitivity pneumonitis, transplantation associated diseases such as graft rejection or graft-versus-host-disease

FEATURES Location/Qualifiers
CDS 79..1011
/*tag= a
/product= "Human PRO4405 protein"
sig_peptide 79..180
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mat_peptide 181..1008
/*tag= c
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BASE COUNT 566 a 605 c 656 g 568 t
ORIGIN

2395 100 0.0
P_AAF92127 Human PRO4405 cDNA. 395 bp, cDNA, PAT 15-MAY-2001
ACCESSION P_AAF92127
KEYWORDS GENESEQ; Human; PRO protein; mapping; patent; patentdb (v200423, 04-NOV-2004).
SOURCE Homo sapiens.
ORGANISM Homo sapiens.
REFERENCE 1 (bases 1 to 2395)
AUTHORS Eaton,D.L., Filvaroff,E., Gerritsen,M.E., Goddard,A., Godowski,P.J. Grimaldi,C.J., Gurney,A.L., Watanabe,C.K., Wood,W.I.
TITLE Eighty four nucleic acids encoding PRO polypeptides, useful in molecular biology, including use as hybridization probes, and in chromosome and gene mapping.
JOURNAL Patent: WO200116318-A2; Filing Date: 24-AUG-2000; 2000WO-US023328; Publication Date: 08-MAR-2001; Priority: 01-SEP-1999; 99WO-US020111. 15-SEP-1999; 99WO-US021090. 07-DEC-1999;

99US-0169495P. 09-DEC-1999; 99US-0170262P. 11-JAN-2000;
2000US-0175481P. 18-FEB-2000; 2000WO-US004341. 18-FEB-2000;
2000WO-US004342. 22-FEB-2000; 2000WO-US004414. 01-MAR-2000;
2000WO-US005601. 03-MAR-2000; 2000US-0187202P. 21-MAR-2000;
2000US-0191007P. 30-MAR-2000; 2000WO-US008439. 25-APR-2000;
2000US-0199397P. 22-MAY-2000; 2000WO-US014042. 05-JUN-2000;
2000US-0209832P; Assignee: (GETH) GENENTECH INC; Cross Reference:
WPI; 2001-183260/18. P-PSDB; AAB87595; Patent Format: Claim 2; Fig
139; 278pp; English.

COMMENT The present sequence is the coding sequence for a human PRO polypeptide (secreted and transmembrane). The PRO protein, and PRO agonists, PRO antagonists or anti-PRO antibodies are useful for preparation of a medicament useful in the treatment of a condition which is responsive to the PRO protein, agonists, antagonists or anti-PRO antibodies. The PRO protein may also be employed as molecular weight markers for protein electrophoresis. The PRO coding sequence has applications in molecular biology, including use as hybridisation probes, and in chromosome and gene mapping

FEATURES Location/Qualifiers

BASE COUNT 566 a 605 c 656 g 568 t

ORIGIN

2395 100 0.0

P_AAC91490 Human PRO4405 cDNA. 395 bp, cDNA, PAT 21-MAR-2001

ACCESSION P_AAC91490

KEYWORDS GENESEQ; Human; PRO; antiinflammatory; dermatological; antiarthritic; antirheumatic; cardiant; antianaemic; immunosuppressive; antithyroid; antidiabetic; nootropic; neuroprotective; hepatotropic; virucide; antiallergic; antiasthmatic; immune related disorder; hepatobiliary disease; autoimmune disease; allergy; patent; patentdb (v200423, 04-NOV-2004).

SOURCE Homo sapiens.

ORGANISM Homo sapiens.

REFERENCE 1 (bases 1 to 2395)

AUTHORS Ashkenazi,A.J., Baker,K.P., Chan,B., Goddard,A., Godowski,P.J. Gurney,A.L., Hebert,C., Henzel,W., Kabakoff,R.C., Shelton,D.L., Tumas,D. Watanabe,C.K., Wood,W.I.

TITLE Thirty three nucleic acids encoding PRO polypeptides which are useful in the diagnosis and treatment of immune related disorders, e.g. systemic lupus erythematosis, rheumatoid arthritis, osteoarthritis, thyroiditis and diabetes mellitus.

JOURNAL Patent: WO200073452-A2; Filing Date: 02-JUN-2000; 2000WO-US015264; Publication Date: 07-DEC-2000; Priority: 02-JUN-1999;
99WO-US012252. 20-JUL-1999; 99US-0144732P. 20-JUL-1999;
99US-0144758P. 28-JUL-1999; 99US-0146222P. 01-SEP-1999;
99WO-US020111. 15-SEP-1999; 99WO-US021090. 15-SEP-1999;
99WO-US021547. 29-OCT-1999; 99US-0162506P. 30-NOV-1999;
99WO-US028313. 01-DEC-1999; 99WO-US028634. 02-DEC-1999;
99WO-US028551. 02-DEC-1999; 99WO-US028565. 09-DEC-1999;
99US-0170262P. 20-DEC-1999; 99WO-US030911. 05-JAN-2000;
2000WO-US000219. 06-JAN-2000; 2000WO-US000376. 11-FEB-2000;
2000WO-US003565. 18-FEB-2000; 2000WO-US004341. 18-FEB-2000;
2000WO-US004342. 22-FEB-2000; 2000WO-US004414. 24-FEB-2000;
2000WO-US004914. 24-FEB-2000; 2000WO-US005004. 01-MAR-2000;
2000WO-US005601. 02-MAR-2000; 2000WO-US005841. 03-MAR-2000;
2000US-0187202P. 15-MAR-2000; 2000WO-US006884. 20-MAR-2000;

2000WO-US007377. 21-MAR-2000; 2000WO-US007532. 30-MAR-2000;
2000WO-US008439. 17-MAY-2000; 2000WO-US013705. 22-MAY-2000;
2000WO-US014042; Assignee: (GETH) GENENTECH INC; Cross Reference:
WPI; 2001-025253/03. P-PSDB; AAB50931; Patent Format: Claim 48; Fig
59; 218pp; English.

COMMENT The present sequence is one of thirty three nucleic acids encoding PRO polypeptides. The PRO polypeptides, anti-PRO antibodies, agonists and antagonists are useful for treating and diagnosing immune related disorders such as systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis, idiopathic inflammatory myopathies, Sjogren's syndrome, systemic vasculitis, sarcoidosis, autoimmune haemolytic anaemia, autoimmune thrombocytopaenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, demyelinating diseases of the central and peripheral nervous systems (such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barre syndrome, and chronic inflammatory demyelinating polyneuropathy), hepatobiliary diseases (such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis and sclerosing cholangitis), inflammatory bowel disease, gluten-sensitive enteropathy and Whipple's disease, autoimmune or immune-mediated skin diseases (such as bullous skin diseases, erythema multiforme, contact dermatitis, psoriasis), allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria), immunological diseases of the lung (such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis), transplantation associated diseases including graft rejection and graft-versus-host diseases

FEATURES Location/Qualifiers

BASE COUNT 566 a 605 c 656 g 568 t

ORIGIN

2395 100 0.0

AX089946 Sequence 7 from Patent WO0116319. 2395 bp, DNA, linear, PAT 21-MAR-2001

ACCESSION AX089946

VERSION AX089946.1 GI:13443984

KEYWORDS .

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1

AUTHORS Goddard,A., Godowski,P.J., Gurney,A.L., Hillan,K.J., Tumas,D., Watanabe,C.K. and Wood,W.I.

TITLE Compositions and methods for the treatment of immune related diseases

JOURNAL Patent: WO 0116319-A 7 08-MAR-2001; Genentech, Inc. (US)

FEATURES Location/Qualifiers

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BASE COUNT

ORIGIN

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2395 100   0.0
AX092408    Sequence 139 from Patent WO0116318. 2395 bp,
          DNA, linear, PAT 21-MAR-2001
ACCESSION   AX092408
VERSION     AX092408.1  GI:13444518
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
          Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
          Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1
  AUTHORS   Eaton,D.L., Filvaroff,E., Gerritsen,M.E., Goddard,A.,
          Godowski,P.J., Grimaldi,C.J., Gurney,A.L., Watanabe,C.K. and
          Wood,W.I.
  TITLE     Secreted and transmembrane polypeptides and nucleic acids encoding
          the same
  JOURNAL   Patent: WO 0116318-A 139 08-MAR-2001;
          Genentech, Inc. (US)
FEATURES             Location/Qualifiers
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BASE COUNT
ORIGIN

2395 100   0.0
AX055478    Sequence 108 from Patent WO0073452. 2395 bp,
          DNA, linear, PAT 13-JAN-2001
ACCESSION   AX055478
VERSION     AX055478.1  GI:12228736
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
          Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
          Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1
  AUTHORS   Ashkenazi,A.J., Baker,K.P., Chan,B., Goddard,A., Godowski,P.J.,
          Gurney,A.L., Hebert,C., Henzel,W., Kabakoff,R.C., Shelton,D.L.,
          Tumas,D., Watanabe,C.K. and Wood,W.I.
  TITLE     Compositions and methods for the treatment of immune related
          diseases
  JOURNAL   Patent: WO 0073452-A 108 07-DEC-2000;
          Genentech, Inc. (US)
FEATURES             Location/Qualifiers
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ORIGIN
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